

**REMARKS**

Claims 11, 12, 14, 15, 17, 18, 33-35, 37, 38, 47, 48, 50 and 52-55 are cancelled. Claim 31 is withdrawn. Claims 1, 2, 19, 20, 21, 27, 30, 40, 43-46, 49, 51, 56 and 57 are amended. New claims 62 and 63 have been added. Claims 1-10, 13, 16, 19-30, 32, 36, 39-46, 49, 51 and 56-63 are now pending. Reconsideration is respectfully requested in view of the following remarks.

**I. Claim Objection**

Applicant amended claim 57 as suggested by the Examiner. Withdrawal of the above claim objection is therefore respectfully requested.

**II. Specification Objection**

Examiner objected to amendment filed September 10, 2002, paper 16, because according to the Examiner, the amendment introduces new matter into the disclosure. Applicant has deleted the phrase "the disclosure of which is incorporated herein by reference in its entirety" as requested by the Examiner. Withdrawal of the above specification objection is therefore respectfully requested.

**II. Claim Rejections Under 35 U.S.C. 112, First Paragraph**

The Examiner rejected claims 1-10, 13, 14, 16-34, 36-46, 49, 51 and 56-61 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In particular the Examiner asserts that while "[t]he specification reduces to practice the claimed invention with the compound sulfosccinimidyl-2(biotinamidoethyl-1,3dithiopropionate, [] there is no specific teaching for other compounds with these specific properties recited in the claims, nor is there general teaching or evidence of how or what feature of sulfosccinimidyl-2(biotinamidoethyl-1,3dithiopropionate is representative of the genus of the elected species or other cleavable moieties." Office Action, p. 6..

Applicants respectfully traverse the Examiner's rejection under 35 U.S.C. 112, first paragraph for the following reasons. First, the specification does teach a variety of compounds that have properties similar to that sulfosccinimidyl-2(biotinamidoethyl-1,3dithiopropionate. In

particular, the specification provides that the compounds herein have a third domain, which is a cleavable chemical moiety domain. The cleavable chemical moiety domain, according to the specification, will not cleave under *in vivo* conditions. (See page 16). Examples of cleavable chemical moieties include disulfide groups, “with exemplary conditions for cleavage including, e.g., at 37°C with about 10 to 50 mm dithiothreitol (DTT) at pH 8.5 within 30 minutes” or “disulfides also cleaved with, e.g., about 1% to about 5% β-mercaptoproethanol (2-ME).”

In addition to the disulfide group cleavable chemical moiety, the specification discloses additional cleavable chemical moieties, such as periodate-cleavable glycol, dithionite-cleavable diazobond, hydroxylamine-cleavable ester, and base-labile sulfone. See Specification, p. 5. A person of ordinary skill in the art is familiar with the above cleavable moieties and their cleaving conditions.

The Examiner has not provided sufficient reason to doubt that a person of ordinary skill in the art would not be able to identify the genus that these cleavable chemical moieties belong to. Therefore, Applicants respectfully request that the rejection under 35 U.S.C. 112, first paragraph, be withdrawn.

### **III. Claim Rejections Under 35 U.S.C. 112, Second Paragraph:**

The Examiner rejected claims 1-10, 13, 14, 16-34, 36-46, 49, 51, and 55-61 under 35 U.S.C. 102, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

In particular, the Examiner states that, “it is unclear what the metes and bounds of this [non-denaturing] condition would be.” *See* Office Action, at 9. According to the Examiner, “the term denaturing is generally reserved and used to describe proteins and it is unclear what it encompasses relative to other molecules identifiable on the cell.” *Id.*

Applicants respectfully traverse the Examiner’s rejection. As currently amended, independent claims 1, 19 and 51 refer only to lumen exposed proteins, and not to other lumen exposed molecules. Therefore, Applicants respectfully request that the Examiner withdraw the above rejection.

Application No. 09/528,742  
Amendment dated April 1, 2004  
Reply to Office Action of January 9, 2004

**IV. Claim Rejections Under 35 U.S.C. 103(a):**

The Examiner rejected claims 19-34, 36-45, 49, 51, 57, 58, and 61 under 35 U.S.C. 103(a) as being unpatentable over De La Fuente *et al.*, (IDS reference), Hastie *et al.*,(IDS reference), and Rothschild *et al.* (U.S. Patent No. 5,948,624) and Pierce Catalog & Handbook, 1994-1995.

According to the Examiner, “none of the cited reference teach to cleave the molecule under conditions that does not denature the labeled protein.” *See* Office Action, at 11. The Examiner rejected the above claims as unpatentable under 35 U.S.C. 103(a), because according to the Examiner, independent claims 19 and 51 “do not recite such a limitation.”

Applicants respectfully traverse the Examiner’s rejection under 35 U.S.C. 103(a). As currently amended, independent claims 19 and 51 both recite the limitation of “cleaving the cleavable chemical moiety of the reagent that reacted with the lumen exposed protein under a condition that does not denature the lumen-exposed protein.” As such, Applicant respectfully request that the Examiner withdraw the above rejection.

**CONCLUSION**

In light of the remarks set forth above, Applicants believe that they are entitled to a letters patent. Applicants respectfully solicit the Examiner to expedite the prosecution of this patent application to issuance. Should the Examiner have any question, the Examiner is encouraged to telephone the undersigned.

Respectfully submitted,

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